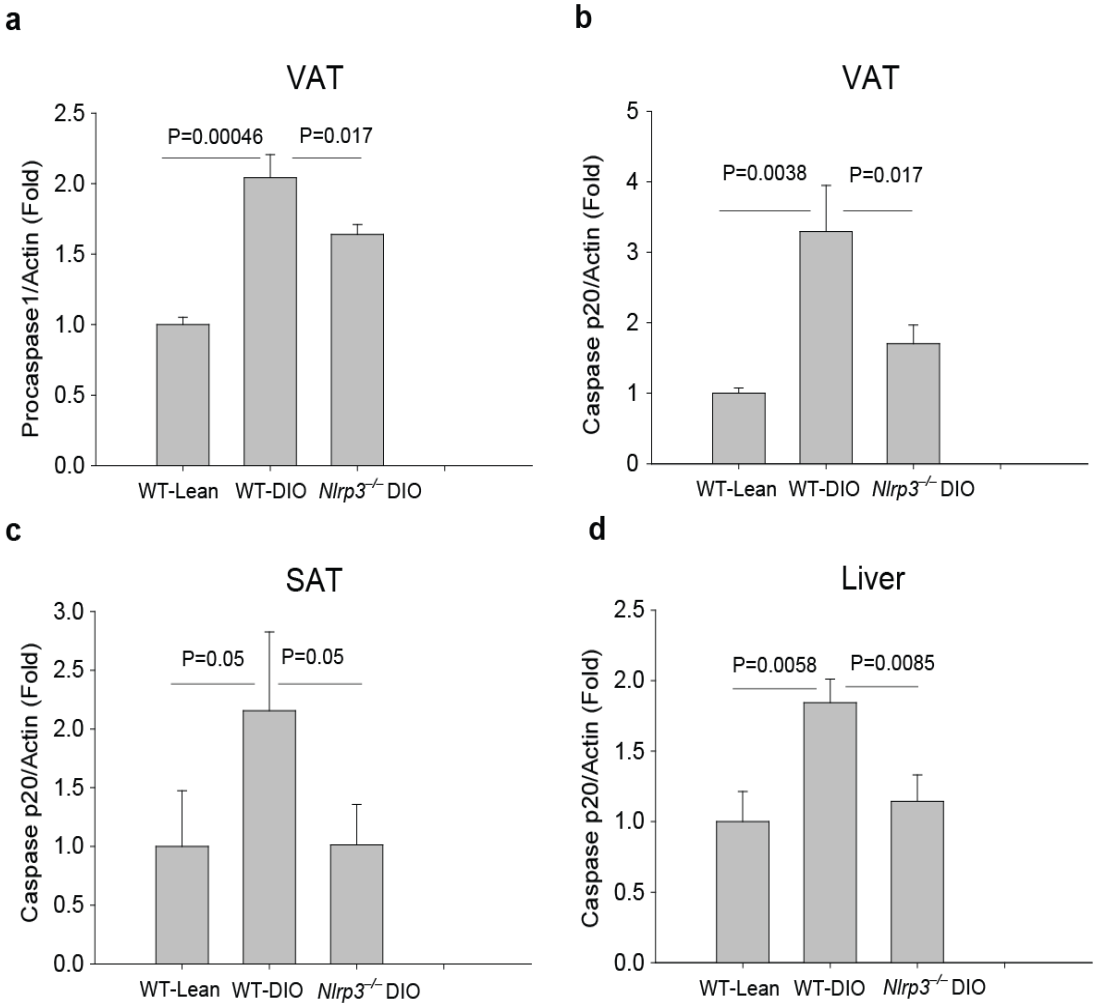
Supplementary Table 1: Subject characteristics

All males and Caucasian
GDR, glucose disposal rate
EMBS, estimated metabolic body size calculated as fat-free mass (kg) + 17.7
*P<0.05 for comparison before and after weight loss in T2D subjects.

	Before	After
Age (years)	61.9±8.7	62.9±8.7
Body weight (kg)	99.9±8.9	88.7±10.6*
BMI (kg/m^2)	32.9±2.9	29.2±3.0*
Body fat (%)	28.8±3.3	24.0±4.0*
HOMA-IR	4.7±2.5	2.6±1.4*
GDR (mg glucose/kg EMBS/min)	4.0±1.3	6.1±1.7*
Fasting glucose (mg/dl)	146±26	118±17*
Fasting FFA (mmol/l)	0.55±0.09	0.44±0.20*
Fasting insulin (mU/l)	12.8±5.5	9.0±4.6*
Fasting adiponectin (µg/ml)	5.7±2.7	7.0±2.2*
Fat cell volume (µl)	0.65±0.10	0.51±0.18*
Relative *NLRP3* mRNA expression in adipose tissue	5.9±2.4	3.0±0.8*
Relative *IL1β* mRNA expression in adipose tissue	2.6±2.2	0.8±0.5

Data are expressed means ± SEM. Covariance analysis was used to compare means between obese type 2 diabetic subjects before and after weight loss. Energy expenditure comparisons were additionally controlled for FFM and FM. Multiple comparisons between groups and time periods (fasting and insulin–stimulated metabolic rates) were adjusted by Tukey–Kramer analysis. *P < 0.05 for comparison between type 2 diabetic subjects before and after weight loss.

Supplementary Figure 1



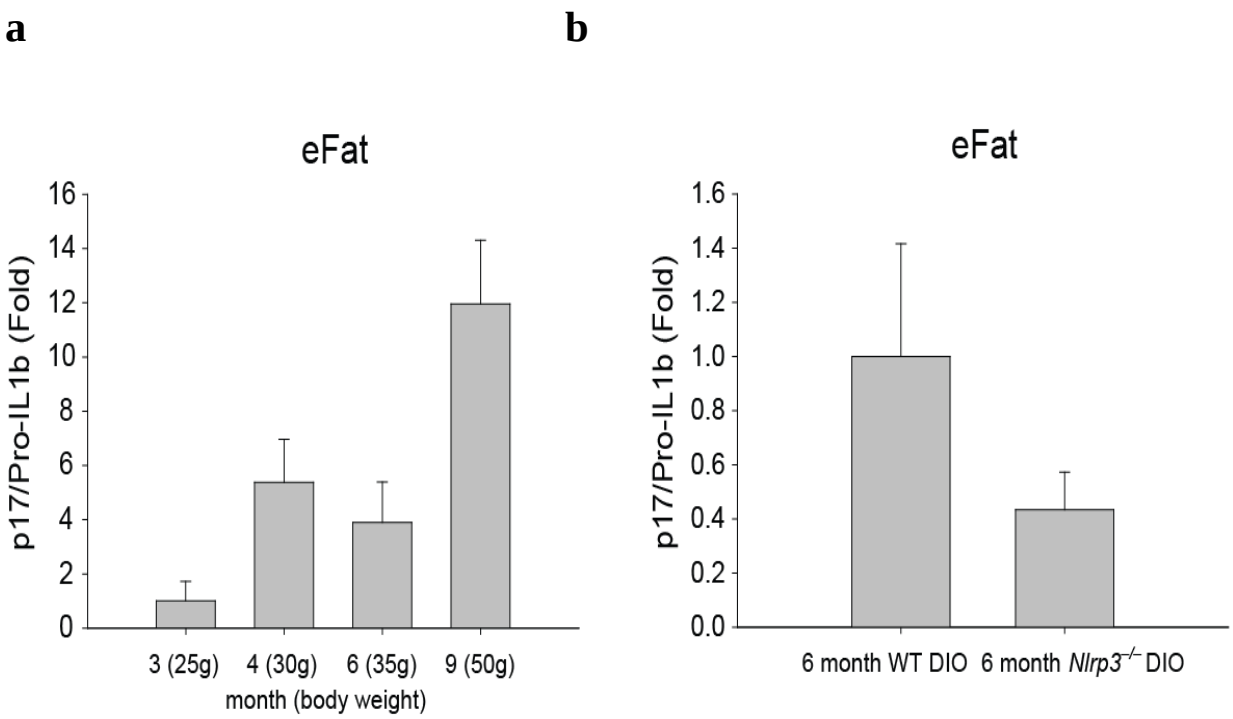
Supplementary Figure 1.

a-b. Quantitation of caspase 1 activation (immunoblots of Figure 2e, upper gel). Obesity increases total procaspase 1 as well as caspase1 activation in VAT, while elimination of Nlrp3 (*P*=0.017) decreases the caspase 1 activity in VAT.

c. Quantitation of caspase 1 activation (immunoblots of Figure 2e, middle gel). Obesity increases caspase 1 activation in SAT, while ablation of Nlrp3 reduces the obesity-induced caspase 1 activation (*P*=0.05).

d. Quantitation of caspase 1 activation (immunoblots of Figure 2e, bottom gel). Obesity increases caspase 1 activation in liver. Ablation of Nlrp3 attenuates the obesity–induced caspase 1 activation in liver (*P*=0.0085).

Supplementary Figure 2

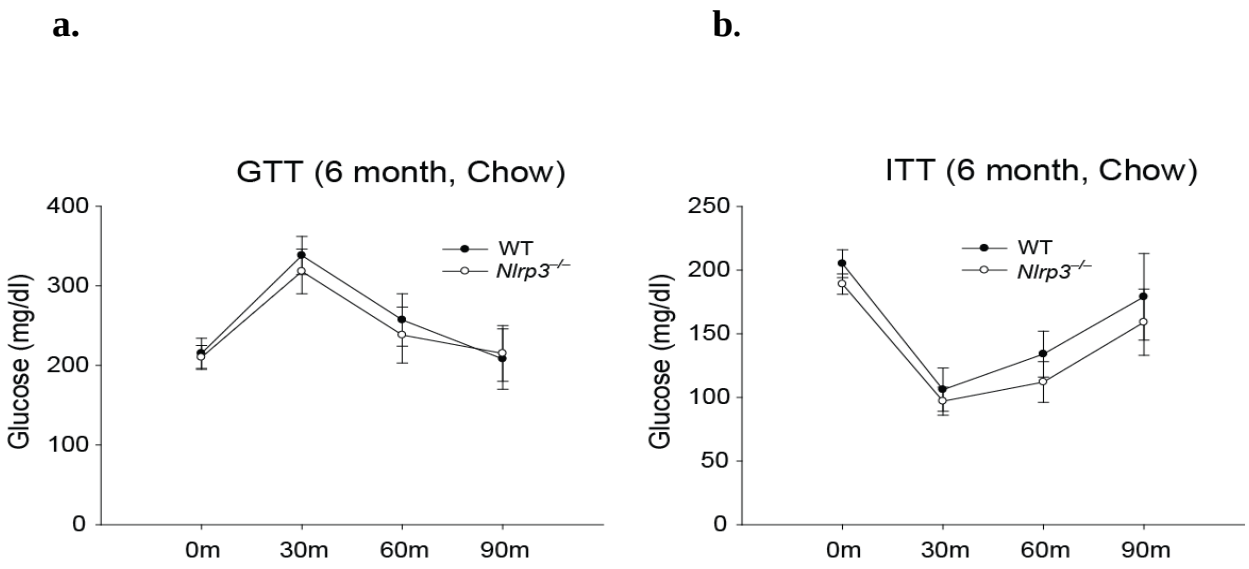


Supplementary Figure 2. Quantitation of the blots and statistical analysis for Figure 2. Densitometry quantifications of the immunoblots were done using Image J software. Results shown are means ± STD.

a. Quantitation of immunoblots in Figure 2d. Progressive adiposity increases IL1β. Quantitation of immunoblots in activation in epididymal fat.

b. Quantitation of immunoblots in Figure 2g. 6 month old Nlrp3$^{-/-}$ DIO mice have lower active p17 form of IL–1β in epididymal fat compared to 6 month old WT DIO mice.

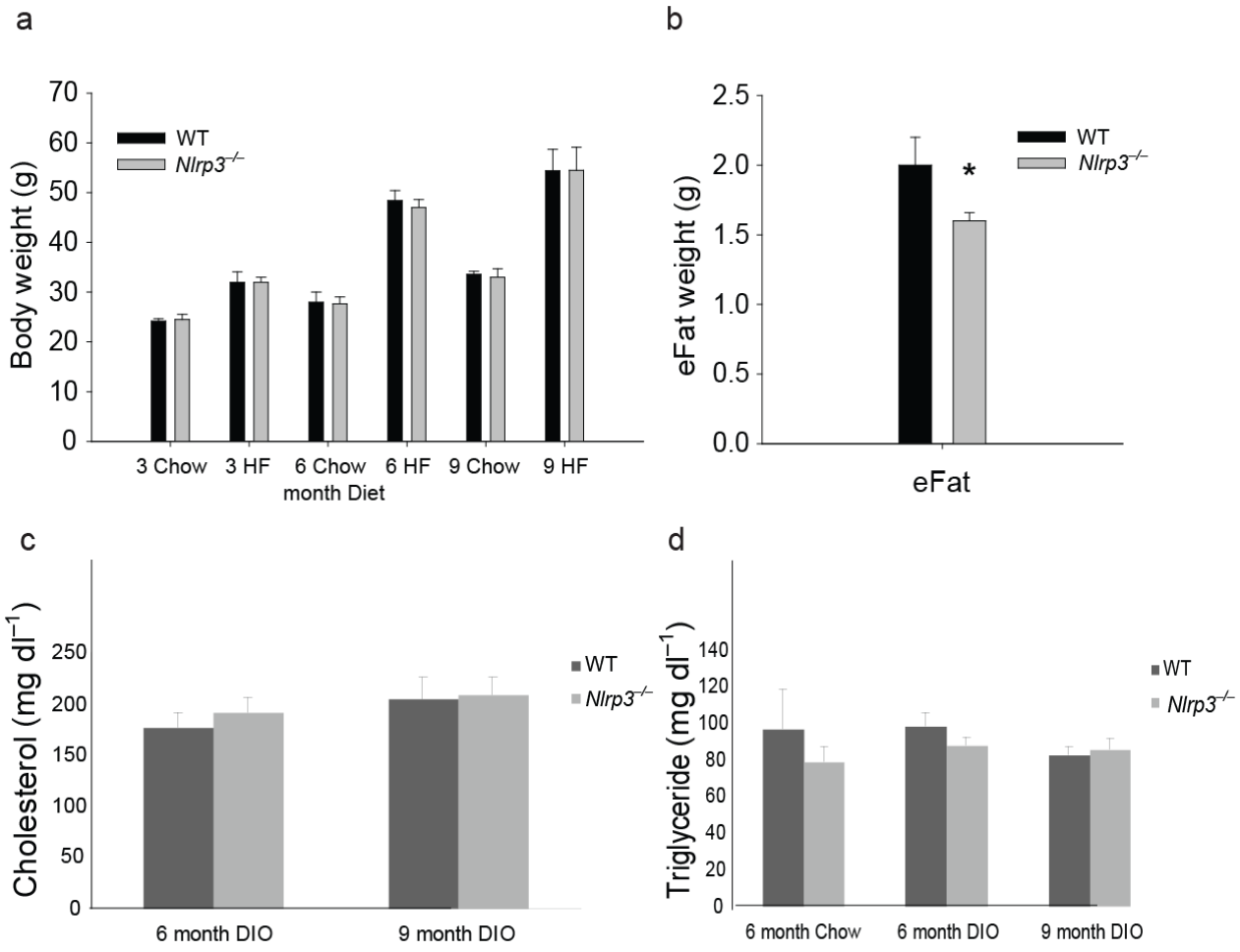
Supplementary Figure 3



Supplementary Figure 3

a-b. GTT and ITT in 6 month old WT (n = 5) and Nlrp3$^{-/-}$ (n = 7) male control (chow diet) mice was conducted in ad libitum fed state. Glucose and Insulin were administered via Intraperitoneal injection (2.0 mg D-glucose g^{-1} body weight and insulin 0.5 mU insulin g^{-1} body weight). Blood glucose levels shown are means ± STD. P values are P = 0.32 to P = 0.72 for GTT and P = 0.098 to P = 0.49 for ITT.

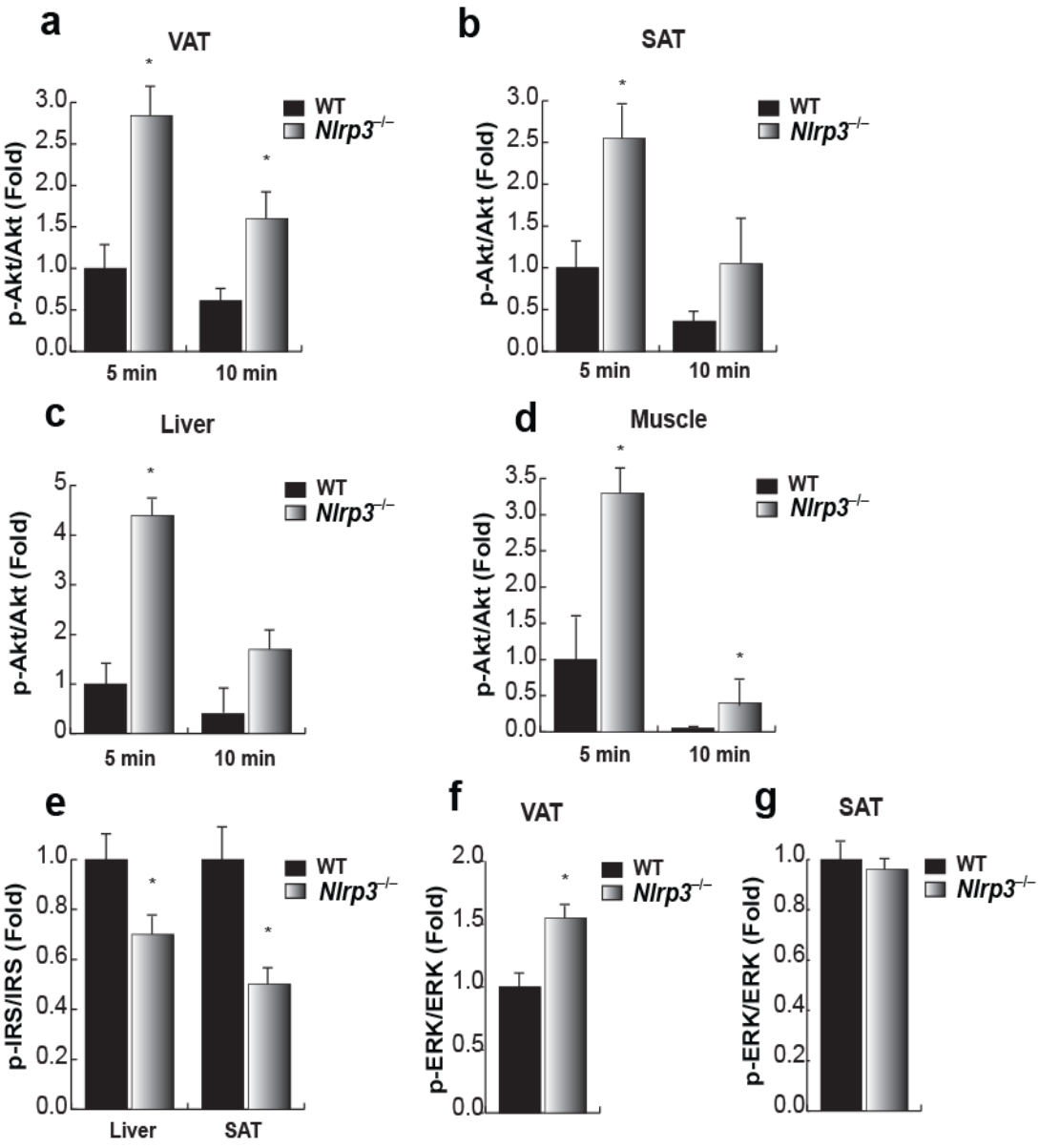
Supplementary Figure 4



Supplementary figure 4.

(a) Body weights of 3, 6 month and 9 month old WT and Nlrp3$^{-/-}$ control and HFD groups. 3 month old WT (6) and Nlrp3$^{-/-}$ (4) male mice were fed a HFD for 6 weeks. 6 month old WT (n = 8) and Nlrp3$^{-/-}$ (n = 8) male mice were fed a HFD for 4 months and 9 month old WT (n = 6) and Nlrp3$^{-/-}$ (n = 5) male mice were fed a HFD for 7 months. P values between groups are P = 0.26 to P = 0.97. **(b)** Epididymal fat (eFat) weight (n = 4–8) in 3 month old male DIO mice fed a HFD for 6 weeks.(**c**) Blood cholesterol and (**d**) triglycerides levels in 6 month and 9 month WT (n = 10 and n = 6) and Nlrp3$^{-/-}$ control and HFD (n = 8 and n = 5) groups. Mice were fasted for 4 hr and blood was collected by cardiac puncture and within 10 seconds 15 µl of whole blood was analyzed for triglyceride and cholesterol using CardioChek Brand Analyzers, Polymer Technology Systems, Inc. Indianapolis, IN, USA. Blood cholesterol levels in 6 month old WT and Nlrp3$^{-/-}$ control (chow) mice were below the detectable range (<100 mg dl^{-1}) for this analyzer. Results shown are means ± SEM. P values between groups are P = 0.11, P = 0.628 and P = 0.662 for triglyceride and P = 0.31 and P = 0.89 for cholesterol.

Supplementary Figure 5

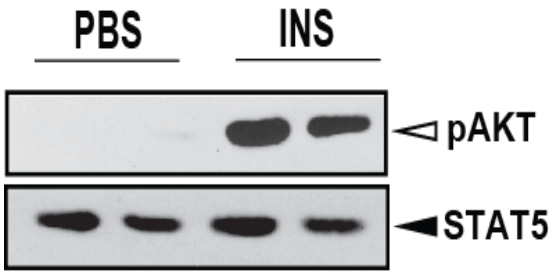


Supplementary figure 5

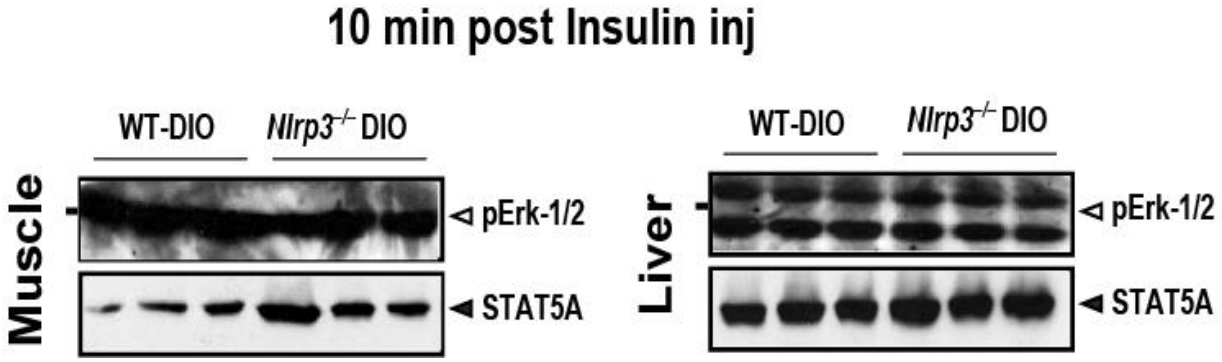
The densitometry analysis of immunblots (Figure 3f) of pAKT, pIRS and pERK after 5 and 10 min insulin injection in 8 month old WT–DIO and Nlrp3$^{-/-}$DIO mice. Densitometry quantifications of the immunoblots were done using Image J software. Results shown are means ± STD, **P*<0.05.

Supplementary Figure 6

a.



b.

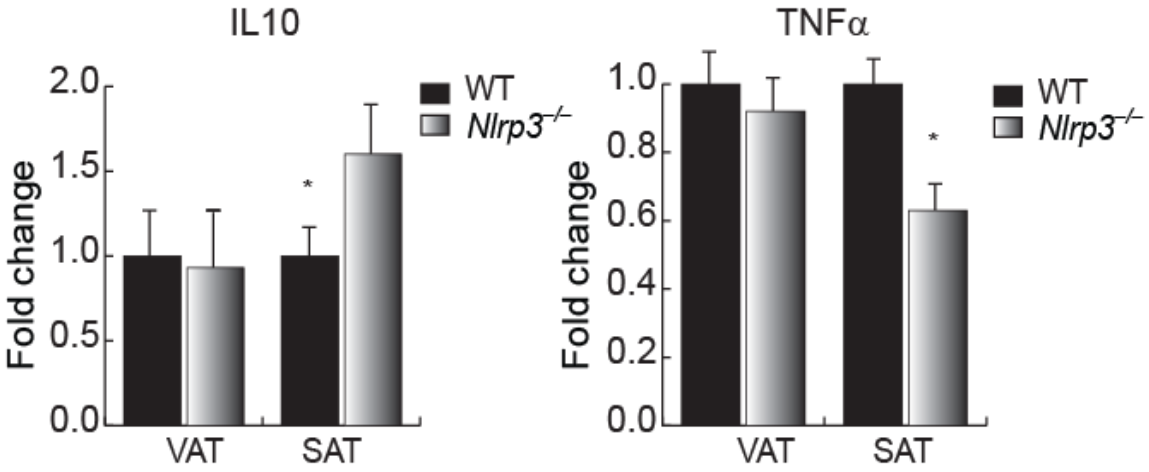


Supplementary figure 6

(**a**) Compared to insulin treated DIO mice, vehicle treated mice did not show any specific AKT phosphorylation.

(**a**) Representative immunoblot of ERK phosphorylation in muscle and liver. Organs were collected 10 min after intraperitoneal insulin injection and snap frozen in liquid nitrogen for western blot analyses. Loss of Nlrp3 function does not affect insulin dependent MAPK activation in muscle and liver.

Supplementary Figure 7



Supplementary figure 7

The Quantitative Real time PCR analysis of cytokine expression in adipose tissue of 9 month old WT and Nlrp3$^{-/-}$ DIO mice (7 months on HFD), (n = 7). Results are shown are means ± STD., *P<0.05.